REMARKS

Claims 1, 3-6, and 8-36 were pending at the time of the Office Action. Claims 33 and 34 have been withdrawn from consideration. Claims 1, 3-5, and 8-20 stand rejected under 35 U.S.C. § 102. Claims 1, 3-6, 8-32, 35, and 36 stand rejected under 35 U.S.C. § 103. Claims 1, 6, 8-32, and 36 are also provisionally rejected for nonstatutory obviousness-type double patenting. Applicant addresses these rejections as follows.

Rejection under 35 U.S.C. § 102

Claims 1, 3-5, and 8-20 stand rejected under 35 U.S.C. § 102(b) as being anticipated by Yanaga et al. (*International Journal of Molecular Medicine* 10: 311-315, 2002; herein "Yanaga"), as evidenced by Dou et al. (U.S. Patent Application Publication No. 2002/0151582; herein "Dou"). According to the Examiner, Yanaga teaches that "EGCG inhibited growth in the mouse viral mammary epithelial carcinogenesis model RIII/MG, and induced apoptosis, suggesting a clinical usefulness of EGCG as a chemopreventive substance" (Office Action, page 4). The Examiner cites Dou as evidentiary support that the green tea extracts of Yanaga contain polyphenolic compounds (e.g., EGCG). This rejection is respectfully traversed.

The present claims are directed to a method of treating precancerous lesions of the skin of a patient (e.g., actinic keratoses) by administration of a polyphenol-containing composition to a patient. In contrast to the pending claims, Yanaga teaches the prevention of viral carcinogenesis in mouse mammary epithelial cells that are initiated with mouse mammary tumor virus (MMTV). This distinction is first highlighted by the title of Yanaga, "Prevention of Carcinogenesis of Mouse Mammary Epithelial Cells RIII/MG by Epigallocatechin Gallate" (emphasis added). Moreover, throughout Yanaga, prevention or protection against subsequent viral carcinogenesis is repeatedly discussed. For example, Yanaga describes the "[p]revention of cancer development by EGCG in RIII/MG-transplanted nude mice" (page 312 of Yanaga, left column) and the inhibition of tumor growth by catechins *in vitro* and *in vivo* (pages 312-313 of Yanaga). Indeed,

Yanaga concludes that "green tea ingested in daily life may be a preventive drug against breast cancer" (page 314 of Yanaga, right column; emphasis added).

Further, with respect to claim 3, Yanaga teaches that RIII/MG cells are generated by infection with mouse mammary tumor virus. In contrast to Yanaga, the precancerous skin lesions (e.g., actinic keratoses) of the present claims are not virally induced. For the record, Applicant notes that catechols (in particular, EGCG) are known to have antiviral properties, most likely due to their inhibitory effect on reverse transcriptase (see, e.g., Yamaguchi et al., *Antiviral Research* 53: 19-34, 2002; herein "Yamaguchi" and submitted with this Reply). Thus, the observed chemopreventive effect of catechins on the RIII/MG and RIII/Pr-1 cells of Yanaga may be the result of the antiviral activity associated with such compounds.

Finally, Applicant notes that the present claims are directed to treating precancerous lesions of the skin of a patient. The RIII mouse mammary epithelial cells used in the experiments of Yanaga are not skin cells, and viral carcinogenesis of RIII mouse mammary epithelial cells would not result in the development of a precancerous skin lesion. For this reason as well, Yanaga fails to anticipate the claims of the present invention.

Yanaga, either alone or as evidenced by Dou, fails to teach all of the elements of claims 1, 3-5, and 8-20, and Applicant respectfully requests that this rejection of the claims under 35 U.S.C. § 102 be withdrawn.

Rejection under 35 U.S.C. § 103

Claims 1, 3-5, and 8-26 stand rejected under 35 U.S.C. § 103(a) as being unpatentable over Yanaga, as evidenced by Dou. This rejection is respectfully traversed. Yanaga, as evidenced by Dou, fails to support a *prima facie* case of obviousness. As described above, Yanaga relates only to the prevention of viral carcinogenesis in mouse mammary epithelial cells initiated with MMTV. Yanaga, alone or in combination with Dou, provides no teaching to suggest that established precancerous lesions of the skin

could, or should, be treated with a polyphenol-containing composition. Specifically, Yanaga does not address treatment of precancerous lesions, does not discuss treatment of the skin, and, with respect to claim 3, does not mention a non-virally induced lesion of any sort. Accordingly, Applicant respectfully requests that the rejection of the claims under 35 U.S.C. § 103(a) be withdrawn.

Claims 1, 3-6, 8-32, and 35 stand further rejected under 35 U.S.C. § 103(a) as being unpatentable over Yanaga in view of Brash et al. (U.S. Patent Application Publication No. 2002/0198161; herein "Brash") and further in view of Voet (U.S. Patent No. 6,723,750; herein "Voet"), as evidenced by Dou. Brash and Voet fail to cure the deficiencies of Yanaga, as neither indicates that polyphenol-containing compounds treat precancerous lesions of the skin. Reconsideration and withdrawal of this second basis for the rejection is also respectfully requested.

Claims 1, 3-6, 8-20, and 36 stand rejected under 35 U.S.C. § 103(a) as being unpatentable over Yanaga and Dou in view of An et al. (*Photochemistry and Photobiology* 76: 73-80, 2002; herein "An"). The Examiner states (Office Action, page 10):

> It would have been *prima facie* obvious for one of ordinary skill in the art at the time the invention was made to use the green tea extract to treat actinic keratoses from [An] since [An] teach[es] green tea extract (1 mg/cm^2) largely abrogated the acute COX-2 response to UVB in mice or humans.

Applicant submits that An fails to cure the deficiencies of Yanaga, as An does not teach or suggest the treatment of precancerous lesions of the skin, such as actinic keratoses. An teaches the topical administration of green tea polyphenol (GTP) extract to murine or human skin prior to UVB irradiation, resulting in the subsequent attenuation of COX-2 expression in the treated cells. An fails to teach or suggest that GTP extract treats an established lesion (e.g., actinic keratoses). Indeed, An states (pages 78-79):

> [T]he observed decrease in COX-2 expression in both murine and human skin receiving a topical application of GTP suggests that GTP may act as a chemopreventive agent by blocking this target.

Accordingly, Applicant respectfully requests that this rejection of claims 1, 3-6, 8-20, and 36 under 35 U.S.C. § 103(a) be withdrawn.

Provisional Double-Patenting Rejection

Claims 1, 6, 8-32, and 36 stand provisionally rejected for obviousness-type double patenting over claims 1-6, 8, 16, 18, 23-27, and 30-33 of co-pending U.S. Patent Application Serial No. 10/682,612. Applicant requests that this rejection be held in abeyance until the pending claims are found to be otherwise allowable except for these grounds of rejection.

CONCLUSION

Applicant submits that the claims are now in condition for allowance, and such Action is respectfully requested.

If there are any charges or any credits, please apply them to Deposit Account No. 03-2095.

Respectfully submitted,

Date: 29 September 2009

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